



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE

United States Patent and Trademark Office

Address: COMMISSIONER FOR PATENTS

P.O. Box 1450

Alexandria, Virginia 22313-1450

www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/727,779	12/03/2003	Shea N. Gardner	IL-11191	7079
24981 7590 09/26/2008 Lawrence Livermore National Security, LLC LAWRENCE LIVERMORE NATIONAL LABORATORY PO BOX 808, L-703 LIVERMORE, CA 94551-0808				
EXAMINER BERTAGNA, ANGELA MARIE				
ART UNIT		PAPER NUMBER		
1637				
MAIL DATE		DELIVERY MODE		
09/26/2008		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

### Office Action Summary

**Application No.**

10/727,779

**Applicant(s)**

GARDNER ET AL.

**Examiner**

ANGELA BERTAGNA

**Art Unit**

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 June 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-11, 16 and 17 is/are pending in the application.
- 4a) Of the above claim(s) 1-10 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 11, 16 and 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/5508)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Status of the Application***

1. Applicant's response filed on June 27, 2008 is acknowledged. Claims 1-11, 16, and 17 are currently pending. In the response, Applicant amended claim 16. Claims 1-10 are withdrawn from consideration as being drawn to a non-elected invention.

The rejection of claim 16 under 35 U.S.C. 112, second paragraph has been withdrawn in view of the amendment.

Applicant's arguments regarding the rejections made under 35 U.S.C. 102(a), 35 U.S.C. 102(e), and 35 U.S.C. 103(a) have been fully considered, but they were not persuasive for the reasons set forth in the "Response to Arguments" section.

This Office Action contains new grounds of rejection in sections 3-9. These new grounds of rejection were necessitated by Applicant's amendment, and therefore, this Office Action is made FINAL.

***Priority***

2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(e) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) and 120 as follows: The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original non-provisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35

U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosures of the prior-filed applications, Application No. 10/394,337 and Provisional Application No. 60/428,579, fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, neither application provides support for the instant claims 16 and 17, because the earlier-filed applications do not teach that the method is conducted using n-mers of a size  $n+1$  or  $n+2$  (claim 16) or that the method is conducted using oligos in multiple reading frames (claim 17). Therefore, since the earlier-filed applications do not provide adequate support for the instant claims 16 and 17, the filing date of the instant application (**December 3, 2003**) has been used for prior art purposes.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> paragraph (New Matter)***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 16 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

As noted in MPEP 2163.06 I, "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)."

Claim 16 is drawn to the method of claim 11, wherein the starting oligos of length  $n$  ( $n$ -mers), where  $n$  is an odd number, have a length of  $n+1$  or  $n+2$ . Claim 16 as originally filed required the starting oligos to have a length  $n+1$ ,  $n+2$ , etc. Therefore, the amendment to claim 16 broadens the scope of the claims by only requiring the starting oligos to have a length of  $n+1$  **or**  $n+2$  rather than lengths of  $n+1$  **and**  $n+2$ , etc.

Applicant's response does not indicate where the amendment finds support in the original disclosure. The specification teaches in paragraphs 63 and 64 that the starting oligos have a length of  $n+1$ ,  $n+2$ , etc, but does not provide support for a broader embodiment of the method wherein starting oligos having a length of  $n+1$  or  $n+2$ , where  $n$  is an odd number, are used to practice the method of claim 11. Therefore, the method of amended claim 16 is not adequately supported by the original disclosure, and it has been rejected under 35 U.S.C. 112, first paragraph for incorporating new matter.

#### *Claim Rejections - 35 USC § 102*

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(c) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an

international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Evans (US 2003/0087238 A1; cited previously). This pre-grant publication was filed August 2, 2001.

Regarding claim 11, Evans discloses a method of producing a DNA molecule of 1-10 kb of user-defined sequence (paragraph 53 teaches production of a 5 kb sequence) comprising:

(a) virtually pre-selecting a multiplicity of DNA segments that will comprise a user-defined DNA molecule by using computational techniques to virtually break the DNA molecule into fragments of defined size (see Figure 3 and paragraphs 58, 82, and 189-195)

(b) providing fragments *in vitro* of length n (n-mers) of defined size that correspond to the virtual fragments (paragraphs 58, 82, and 195)

(c) arraying fragments *in vitro* by arraying the n-mers into groups (see Figure 3 and paragraphs 58, 82, and 195)

(d) separating the n-mers temporally *in vitro* (see paragraphs 58 and 62, where Evans teaches sequential addition of the segments)

(e) assembling the groups *in vitro* into double-stranded DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase to produce the DNA molecule of user-defined sequence (paragraphs 58 and 68 teach assembly using a polymerase; paragraphs 38, 93-98, and 195-199 teach assembly by PCR, which inherently comprises parallel synthesis and shuffling using a DNA polymerase)

wherein the step of separating the DNA sequence segments occurs temporally (see paragraphs 58 and 62) and the step of assembling the groups into double-stranded DNA

molecules of pre-determined base pairs is accomplished by adding the DNA sequence segments gradually, in sequence order (paragraphs 58 and 62).

Further regarding claim 11, Evans teaches that the sequential addition minimizes errors (paragraph 66) and that computational techniques may be use to optimize (*i.e.* minimize errors) in the entire method (paragraph 178). Evans further teaches that the resulting polynucleotide is 5 kb (paragraph 53), which anticipates the claimed size range of 1-10 kb. Evans also teaches that the oligos used in the method have a length  $n$ , which is an odd number (paragraphs 58 & 82)

6. Claims 16 and 17 are rejected under 35 U.S.C. 102(a) and 102(e) as being anticipated by Evans (2003/0087238 A1; published May 8, 2003; filed August 2, 2001; cited previously). As noted above, claims 16 and 17 have not been granted benefit of the earlier filing date of the previously filed provisional and non-provisional applications, but rather the instant application filing date of December 3, 2003. Therefore, these claims are rejected under 102(a) and 102(e).

Regarding claim 16, Evans teaches that the oligonucleotides may be different lengths (paragraph 53). Evans further teaches examples of oligonucleotides with lengths of 15 ( $n$ ), 16 ( $n+1$ ), or 17 ( $n+2$ ) (see paragraph 53).

Regarding claim 17, Evans teaches that the multiplicity of DNA fragments comprises oligos in multiple reading frames. Specifically, Evans teaches variation of the oligo length and overlap between the fragments (paragraphs 53 and 54). These DNA fragments inherently comprise multiple reading frames.

***Claim Rejections - 35 USC § 103***

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 11 and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Selifonov et al. (WO 00/42560; cited previously) in view of Evans (US 2003/0087238 A1; cited previously).

Selifonov discloses a method of making polynucleotides having user-defined characteristics (see for a general description, pages 3-6 “Summary of Invention” and also page 9, lines 23-31).

Regarding claim 11, Selifonov discloses a method of producing a DNA molecule of user-defined sequence comprising:



(a) virtually preselecting a multiplicity of DNA segments that will comprise a user-defined DNA molecule by using computational techniques to virtually break the DNA molecule into virtual fragments of length  $n$  ( $n$ -mers), where  $n$  is an odd number (page 14, lines 20-29 and page 21, lines 12-22 teach using computational methods to virtually break the DNA molecule into virtual fragments; page 6, lines 8-10 teach using  $n$ -mers where  $n$  is an odd number)

(b) providing fragments of length  $n$  ( $n$ -mers) of defined size, where  $n$  is an odd number, that correspond to the virtual fragments (page 9, lines 23-31 and page 21, lines 12-30 teach providing fragments *in vitro* that correspond to the virtual fragments generated in step (a) above; page 6, lines 8-10 teaches using  $n$ -mers where  $n$  is an odd number in the synthesis method)

(c) arraying the fragments of defined size into groups (page 14, lines 27-30, where Selifonov teaches that the fragments may be left with the parental strands or transferred to a new population. Selifonov also teaches formation of new populations; see also page 21, lines 14-15 and lines 23-30, where sets are combined)

(d) separating the DNA sequence segments temporally (page 22, lines 4-19, where Selifonov teaches variation of the composition of fragments in the recombination reaction and/or performing multiple recombination reactions. This is a temporal separation of the DNA segments)

(e) assembling the groups into double-stranded DNA molecules of predetermined base-pairs using parallel synthesis, DNA shuffling, and DNA polymerase to produce the DNA molecule of user-defined sequence (page 21, line 23 – page 22, line 13).

See also Figures 4A-D for a flow-chart depiction of the method of Selifonov.

Further regarding claim 11, Selifonov teaches that the assembled polynucleotide of user-defined sequence is 1.6 kb (page 70), a value within the claimed range of 1-10 kb. Selifonov also teaches computational modeling in an effort to minimize reassembly errors (see for example, page 10, lines 26-33). However, Selifonov does not explicitly teach sequential addition of DNA segments in the reassembly process.

Regarding claim 17, Selifonov teaches that the multiplicity of DNA fragments comprises oligos in multiple reading frames. Specifically, Selifonov teaches variation of the oligo length and overlap between the fragments (page 33, lines 1-6). These DNA fragments inherently comprise multiple reading frames.

Evans teaches a method of synthesizing a user-defined nucleic acid sequence that anticipates the instant claims 11, 16, and 17, as discussed above.

Regarding claim 11, Evans teaches that addition of the oligonucleotides in a sequential order (optimized by computational modeling) minimizes reassembly errors (see paragraphs 58, 66, and 178). Specifically, Evans stated, "The sequential polynucleotide assembly methods of the invention further reduce the error rate observed with methods that require hybridization of pools of large numbers of oligonucleotides (paragraph 66)." Evans further stated, "The sequential polynucleotide assembly methods of the invention eliminate the need for purification and allow for systematic assembly of identical sized double-stranded or single-stranded oligonucleotides (paragraph 66)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to utilize the *in silico*-optimized sequential addition of DNA fragments taught by Evans in the nucleic acid synthesis method of Selifonov. Evans expressly taught the

advantages of sequential addition of oligonucleotide segments in sequence order, namely: (1) a reduction in the assembly error rate, (2) elimination of the need for an extra purification step and (3) parallel synthesis of identical-sized nucleic acids (see paragraph 66 and above). An ordinary artisan would have been motivated by these teachings of Evans to sequentially add the fragments to the reassembly reaction in sequence order in order to improve the accuracy of the reassembly reaction, eliminate the need for further purification (thereby improving the speed and efficiency of the process), and obtain the ability to synthesize in parallel multiple, identically-sized nucleic acids. Thus, the method of the instant claim 11 and 17 is *prima facie* obvious over Selifonov in view of Evans.

9. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Selifonov et al. (WO 00/42560; cited previously) in view of Evans (US 2003/0087238 A1; cited previously) and further in view of Murphy et al. (USPN 6,994,963; cited previously).

The combined teachings of Selifonov and Evans result in the method of claims 11 and 17, as discussed above.

Selifonov teaches variation of DNA segment lengths and the use of a set of DNA segments comprising fragments of different lengths (see page 6, lines 8-10 and page 33, lines 1-6). However, Selifonov does not explicitly teach fragments of  $n+1$  or  $n+2$ .

Murphy teaches a method of nucleic acid recombination. Briefly, the method of Murphy comprises primer extension and cleavage to create an "extension ladder" (column 4, lines 9-16) followed by recombinatorial synthesis to produce a mutagenized or chimeric nucleic acid (column 6, lines 34-40).

Regarding claim 16, Murphy teaches that the “extension ladder” (a collection of DNA segments) may comprise sequences of different length, specifically, sequences different by one nucleotide increments (*i.e.*  $n$ ,  $n+1$  or  $n+2$ ) (see column 6, lines 49-56). Regarding the differently sized sequences, Murphy stated, “Furthermore, the present invention may use a complete library of nucleic acid extension products that differ in length by a single base. As a result, recombinatorial mutagenesis results in recombined sequences with potential crossover points at every single nucleotide in a nucleic acid sequence (column 3, line 66 – column 4, line 4).”

It would have been *prima facie* obvious for one of ordinary skill in the art at the time of invention to utilize DNA fragments differing by one nucleotide in length ( $n$ ,  $n+1$ ,  $n+2$ , etc) in the recombination method resulting from the combined teachings of Selifonov and Evans, since Murphy expressly taught that such a fragment pool resulted in “recombined sequences with potential crossover points at every single nucleotide in a nucleic acid sequence (column 3, line 66 – column 4, line 4).” An ordinary practitioner of the method resulting from the combined teachings of Selifonov and Evans would have been motivated by the teachings of Murphy to utilize the above length-diverse fragment pool in order to maximize the diversity of the resulting recombined/reassembled sequences, thereby improving the method’s ability to generate nucleic acids encoding proteins with improved functional properties. Thus, the method of claim 16 is *prima facie* obvious in view of the combined teachings of Selifonov, Evans, and Murphy.

#### ***Response to Arguments***

10. Applicant’s arguments, see page 11, filed on June 27, 2008, with respect to the rejection of claim 16 under 35 U.S.C. 112, second paragraph have been fully considered and are

persuasive. Applicant's amendment to claim 16 has overcome the rejection, and therefore, it has been withdrawn.

Applicant's arguments filed on June 27, 2008 with respect to the rejection of claim 11 under 35 U.S.C. 102(c) and the rejection of claims 16-17 under 35 U.S.C. 102(a) and 102(c) as being anticipated by Evans have been fully considered, but they were not found persuasive.

Applicant argues that the Evans reference does not teach the following claim limitations: (1) assembling the groups *in vitro* into double-stranded DNA molecules of predetermined base pairs using parallel synthesis, DNA shuffling, and DNA polymerase, (2) adding the DNA sequence segments gradually, in sequence order, (3) adding the DNA segments in an order computationally predicted to minimize errors, (4) that the oligos used in the method have a length  $n$ , which is an odd number, (5) that the oligos used in the method have lengths of  $n+1$  or  $n+2$ , or (6) the oligos used in the method comprise oligos in multiple reading frames (see pages 12-14).

This argument was not persuasive, because as discussed above, Evans teaches all of the aforementioned limitations. Evans teaches *in vitro* assembly using a polymerase at paragraphs 58 & 68. Evans also teaches *in vitro* assembly by PCR, which inherently comprises parallel synthesis and shuffling using a DNA polymerase, at paragraphs 38, 93-98, and 195-199. Evans teaches that the *in vitro* assembly step is conducted by adding the sequence segments gradually in sequence order at paragraphs 58 and 62, for example. Evans further teaches temporal separation of the DNA sequence segments at paragraphs 58 and 62. Evans also teaches that the sequential addition minimizes errors (paragraph 66) and that computational techniques may be used to optimize (*i.e.* minimize errors) in the entire method (paragraph 178). Evans also teaches

that the oligos used in the method have a length  $n$ , which is an odd number, and the use of oligos having a length of  $n+1$  or  $n+2$  (paragraphs 53, 58, & 82). Finally, Evans teaches variation of the oligo length and overlap between the fragments (paragraphs 53 and 54), which inherently results in the use of oligos that comprise multiple reading frames. Thus, Evans teaches all of the elements of the instant claims 11, 16, and 17. Since Applicant's arguments were not found persuasive, the rejections under 35 U.S.C. 102(a) and 102(e) have been maintained.

Regarding the rejection of claims 11 and 17 under 35 U.S.C. 103(a) as being unpatentable over Selifonov in view of Evans and the rejection of claim 16 under 35 U.S.C. 103(a) as being unpatentable over Selifonov in view of Evans and further in view of Murphy, Applicant's arguments filed on June 27, 2008 have been fully considered, but they were not found persuasive. Applicant first argues that the combined teachings of the cited references do not result in the assembling step and final wherein clause in claim 11 or the limitations recited in claims 16 and 17 (see pages 17-18 and 22). This argument was not persuasive, because as discussed above, Evans, Selifonov, and Murphy teach or suggest all of the claimed limitations.

Applicant also argues that the rejections made under 35 U.S.C. 103(a) citing Selifonov and Evans as the primary combination of references fail to meet the teaching-suggestion-motivation (TSM) test and that there are no other reasons for combining the references (see pages 18-19 and 22-23). This argument was not persuasive, because as discussed above, Evans expressly taught the advantages of sequential addition of oligonucleotide segments in sequence order, namely: (1) a reduction in the assembly error rate, (2) elimination of the need for an extra purification step and (3) parallel synthesis of identical-sized nucleic acids (see paragraph 66 and above). An ordinary artisan would have been motivated by these teachings of Evans to

sequentially add the fragments to the reassembly reaction in sequence order in order to improve the accuracy of the reassembly reaction, eliminate the need for further purification (thereby improving the speed and efficiency of the process), and obtain the ability to synthesize in parallel multiple, identically-sized nucleic acids. Also, an ordinary artisan would have been motivated to utilize DNA fragments differing by one nucleotide in length ( $n, n+1$ ) in the recombination method resulting from the combined teachings of Selifonov and Evans, since Murphy expressly taught that such a fragment pool resulted in “recombined sequences with potential crossover points at every single nucleotide in a nucleic acid sequence (column 3, line 66 – column 4, line 4).” An ordinary practitioner of the method resulting from the combined teachings of Selifonov and Evans would have been motivated by the teachings of Murphy to utilize the above length-diverse fragment pool in order to maximize the diversity of the resulting recombined and/or reassembled sequences, thereby improving the method’s ability to generate nucleic acids encoding proteins with improved functional properties. Additionally, Applicant should note that the recent *KSR v. Teleflex* decision forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision *Ex parte Smith*, -- USPQ2d--, slip op. at 20, (Bd. Pat. App. & Interf. June 25, 2007) (citing *KSR*, 82 USPQ 2d at 1936).

Furthermore, in response to Applicant's argument that the Selifonov reference is nonanalogous art (see pages 19-20 and 23-24), it has been held that a prior art reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the applicant was concerned, in order to be relied upon as a basis for rejection of the claimed invention. See *In re Oetiker*, 977 F.2d 1443, 24 USPQ2d 1443 (Fed.

Cir. 1992). In this case, the Selifonov reference and the Evans reference are both directed to *in vitro* methods of shuffling and recombining nucleic acids. Although the Selifonov reference discusses *in silico* methods of shuffling and recombining nucleic acids, the reference also teaches that the method comprises *in vitro* steps in addition to *in silico* steps (see Figures 1B & 4A, page 6, lines 8-26, and page 22, lines 12-18, for example).

Finally, in response to Applicant's argument that the Selifonov and Evans references do not recognize the problem solved by the claimed methods (see page 19), the fact that Applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Since Applicant's arguments were not found persuasive, the rejections of claim 11, 16, and 17 made under 35 U.S.C. 103(a) have been maintained.

### ***Conclusion***

11. No claims are currently allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period



will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANGELA BERTAGNA whose telephone number is (571)272-8291. The examiner can normally be reached on M-F, 9- 5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Kenneth R Horlick/  
Primary Examiner, Art Unit 1637

/ANGELA BERTAGNA/  
Examiner, Art Unit 1637